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Heparin versus normal saline for the care of peripheral intravenous catheters in children: A meta-analysis

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Abstract

Aim: To conduct a meta-analysis to evaluate the role of heparin versus normal saline lock in the care of peripheral intravenous catheters.

Design: A meta-analysis.

Methods: This meta-analysis searched nine databases for randomized controlled trials (RCTs) on heparin versus normal saline for the care of peripheral intravenous catheters in children up to April 5, 2023. The quality of included RCTs was evaluated using the risk of bias tool of Cochrane library. RevMan5.3 software was used for data analysis.

Results: Ten RCTs with a total of 1255 children were involved. Meta-analysis indicated that heparin lock reduced the incidence of blockage of peripheral intravenous catheter [OR = 2.01, 95% CI (1.42,2.84), $p < 0.001$], prolonged the duration of peripheral intravenous catheter indwelling[MD = -0.43, 95% CI (−0.75, −0.11), $p = 0.008$]. There were no statistical differences in the incidence of phlebitis [OR = 1.02, 95% CI (0.59, 1.74), $p = 0.95$ W].

Public contribution: Heparin may have more benefits in the nursing care of peripheral intravenous catheters compared with normal saline.

KEYWORDS

care, children, heparin, normal saline, nursing, peripheral intravenous catheters

1 | BACKGROUND

Peripheral intravenous catheter is the most commonly used peripheral indwelling needle in clinic. It is a transfusion device with a length of 2–6 cm through the peripheral vein, and the end of the catheter is located in the peripheral vein (Alberto et al., 2023). Peripheral intravenous catheter is mainly used for clinical short-term drug infusion, but due to the different stages of children's growth and development, the direction of blood vessels in children is not clear. The puncture and catheter lock techniques in children are different, the outcomes of children with peripheral intravenous catheters are also different (Marsh et al., 2023; Xu et al., 2023). After indwelling peripheral intravenous catheter, it may have related complications, such as phlebitis, drug exudation, catheter blockage and so on, resulting in having to remove peripheral intravenous catheters and increase the pain of re-puncture (Corley et al., 2023; Good et al., 2023). Therefore, the nursing of peripheral intravenous catheters is of great significance to the prognosis of children.

At present, there is still controversy about which kind of fluids to choose for care of peripheral intravenous catheters in children. In the 2021 Infusion Therapy Standards of Practice (Gorski et al., 2021), there is no clear recommendation for which fluid is selected for

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children. The lock solution commonly used in pre-clinical practice is mainly normal saline and heparin sodium solution of different concentration. Normal saline can maintain extracellular fluid volume and osmotic pressure, which is closely associated with the balance of sodium and water in the body and blood circulation (Goossens, 2015; Thorpe et al., 2021). Its advantage is that the normal saline use is not limited by the type of disease, it is especially suitable for patients with bleeding tendency, disturbance of blood coagulation mechanism and insufficiency of liver and kidney (Lok et al., 2020). Heparin saline is a highly effective anticoagulant. Heparin sodium can reduce venous thrombosis and maintain vascular patency, which means that heparin sodium salt solution as a flushing and sealing solution is more and more accepted by nurses (Cook et al., 2011; Lopez-Briz et al., 2022). At present, there are more and more studies on the lock effect of indwelling needle, but no consensus has been reached on which kind of lock solution can reduce the incidence of blockage and phlebitis and prolong the indwelling time. Previous studies (Luo et al., 2013; Qin et al., 2021) have evaluated the selection of lock solution for peripheral intravenous catheters, but the conclusions are inconsistent. Besides, the previous meta-analysis are mostly focused on the adult population, but there are few systematic reviews in the child population. Therefore, it is necessary to systematically search the literature on the basis of the previous published researches, and to evaluate the selection of heparin versus normal saline for the care of peripheral intravenous catheters in children, to provide evidence guidance for clinical peripheral intravenous catheters nursing care.

2 | METHODS

This present meta-analysis was conducted and reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA)statement (Liberati et al., 2009).

We systematically searched the following databases: Web of Science, Embase, Ovid, Cochrane library, Medline, China Biomedical Literature Service system, China knowledge Network, Wanwang and Weipu database. We searched these databases for randomized controlled trials (RCTs) on heparin versus normal saline for the care of peripheral intravenous catheters in children from the establishment of the database to April 5, 2023. The search strategies were as follows: ("peripheral intra venous catheter" OR "peripheral indwelling needle" OR "PIVC" OR "intravenous indwelling needle" OR "venous catheter") AND ("Heparin" OR "sodium chloride" OR "normal saline" OR "heparin sodium" OR "flushing" OR "lock") AND ("child" OR "children" OR "pediatric" OR "infant" OR "newborn"). The languages of the documents searched were limited to Chinese and English. In addition, we analysed and traced the references included in RCTs and related reviews, or database hints of highly relevant literature, in order to include more eligible RCTs.

The inclusion criteria of this literature were as follows: the children were less than 18 years old and were treated with peripheral venous indwelling needle. The study was designed as RCT. Heparin was used to lock the catheter in the intervention group and normal saline was used in the control group. The paper reported the relevant outcome indicators, such as incidence of blockage of peripheral intravenous catheter, the incidence of phlebitis, duration of peripheral intravenous catheter indwelling. We excluded reviews, case studies, and the studies that we could not extract data from the outcome indicators.

The research quality of included RCTs was evaluated according to the quality evaluation standard of Cochrane Handbook for Systematic Review of Intcrventions (Version 5.1.0). The evaluation contents of the tool were as follows: (1) whether the random method was correct; (2) whether the allocation was hidden; (3) whether the blind method was used; (4) reports of withdrawal or loss of follow-up, including the number and causes of loss of follow-up; (5) intention-to-treat (ITT) analysis; (6) baseline comparability. The literature screening and quality evaluation were carried out independently by two researchers, and if they had different opinions, the differences were resolved through discussion or the judgement of the third author. The data extracted from this meta-analysis include author, year of publication, country, number of subjects, age, intervention details and outcome indicators.

The meta-analysis was performed with RevMan5.3 software for synthesized outcomes. Mean difference (MD) or standardized mean difference (SMD) and its 95%confidence interval (CI) were used for measurement data, and ratio (OR) and 95%CI were used as statistics for curative effect analysis. Chi-square test was used to evaluate whether there was heterogeneity in the synthesized result. If $p > 0.1$ and $I^2 < 50\%$, it was considered to be homogeneous, and a fixed effect model was selected for analysis. If $p < 0.0.1$ and $I^2 > 50\%$, heterogeneity was considered, and random effect model was selected. Funnel plots and Egger tests were performed to evaluate the publication bias of synthesized outcomes. $p < 0.0.05$ indicated that there was statistical differences between groups.

3 | RESULTS

As shown in Figure 1, a total of 157 articles were retrieved at the beginning of this meta-analysis, and 38 articles were initially included by reading topics and abstracts, excluding reviews, case reports, repeated publications and those that did not meet the inclusion criteria. After reading the full text, 10 RCTs (Arnts et al., 2011; Dai et al., 2016; Fu et al., 2016; Li et al., 2014; Liang et al., 2019; Upadhyay et al., 2015; Xu, 2012; Yang, 2013; Zhou et al., 2016; Zhou, 2016) were finally included.

As indicated in Table 1, of the included 10 RCTs (Arnts et al., 2011; Dai et al., 2016; Fu et al., 2016; Li et al., 2014; Liang et al., 2019; Upadhyay et al., 2015; Xu, 2012; Yang, 2013; Zhou et al., 2016; Zhou, 2016), a total of 1255 children were involved, of whom 614 children received normal saline lock for peripheral intravenous catheter, 641 children received heparin lock for peripheral intravenous catheter. Most of the included studies were conducted in the department of paediatrics in general hospitals, with children aged from 1 to 12 years old. 24G catheter size is the most commonly

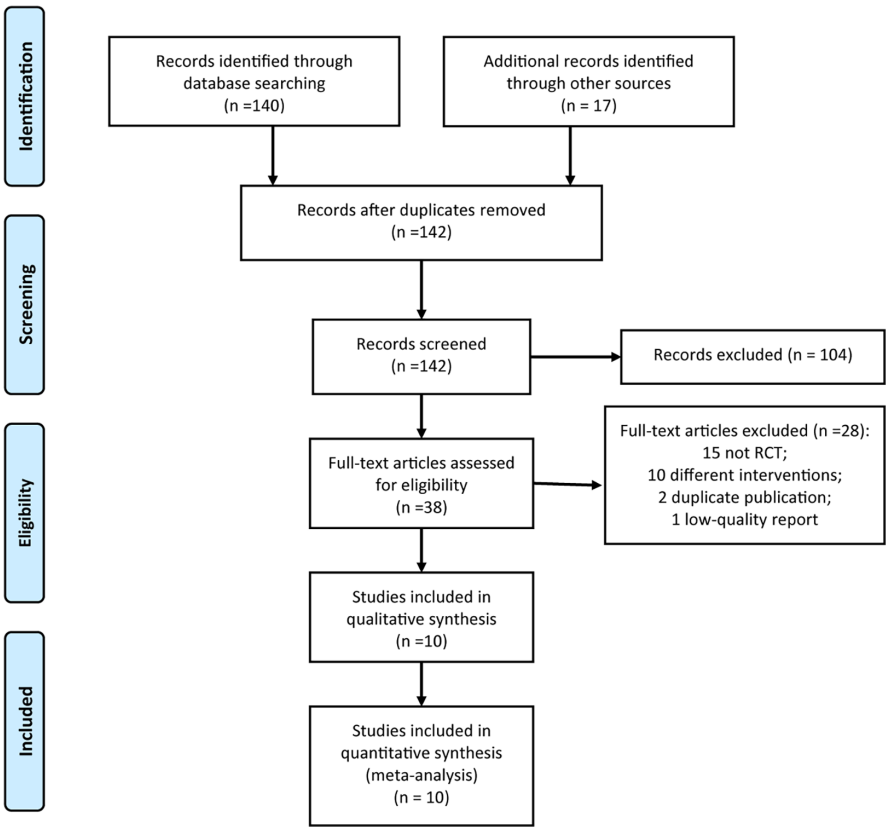


FIGURE 1 PRISMA flow diagram of study inclusion.

used size among the included RCTs. And 10~20 U/mL heparin were the commonly used concentration for the lock for peripheral intravenous catheter.

Table 1 The characteristics of included studies.

As shown in Figures 2 and 3, the 10 included RCTs all mentioned the use of random grouping methods, but one RCT did not mention specific random grouping methods. None of the seven studies mentioned whether to implement allocation concealment. Because of the nature of catheter lock intervention, it is difficult to implement blind method for interventionists, children and outcome evaluators. Each study mentioned that the baseline data of the two groups were comparable. No studies that were in high risk of bias in other items.

Incidence of blockage of peripheral intravenous catheter All the 10 RCT reported incidence of blockage of peripheral intravenous catheter, and there was no statistical heterogeneity among the results ($p=0.19$, $I^2=28\%$), so the fixed effect model was used for meta-analysis. The results showed that the incidence of blockage of peripheral intravenous catheter in the heparin group was lower than that of normal saline group[OR=2.01, 95% CI (1.42,2.84), $p<0.0.001$, Figure 4a].

The incidence of phlebitis Eight RCT included reported the incidence of phlebitis, and there was no statistical heterogeneity among the results ($p=0.72$, $I^2=0\%$), so the fixed effect model was used for meta-analysis. The results showed that there were no statistical differences in the incidence of phlebitis between the heparin group and normal saline group[OR=1.02, 95% CI (0.59, 1.74), $p=0.95$, Figure 4b].

Duration of peripheral intravenous catheter indwelling(days) Eight RCT included reported the duration of peripheral intravenous catheter indwelling, and there was statistical heterogeneity among the results ($p=0.72$, $I^2=0\%$), so the random effect model was used for meta-analysis. The results showed that the duration of peripheral intravenous catheter indwelling in the heparin group was statistically significant longer than that of normal saline group [MD=−0.43, 95% CI (−0.75, −0.11), $p=0.008$, Figure 4c].

As shown in Figure 5, the dots in the funnel plots of synthesized outcomes were evenly distributed, and the results of Egger tests indicated that there were no publication biases(all $p>0.05$).

4 | DISCUSSION

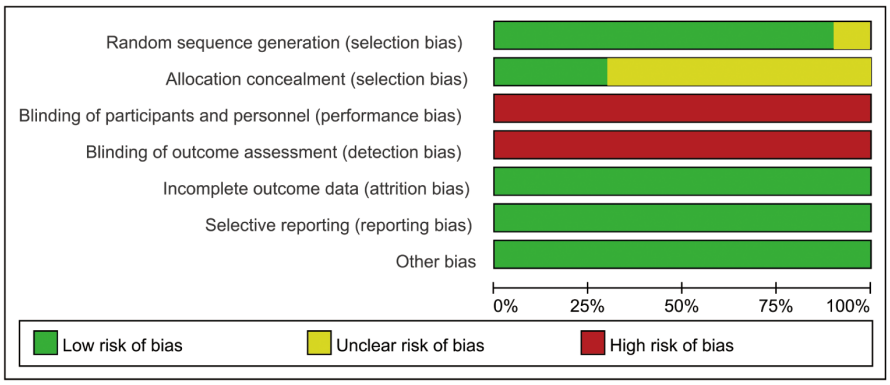
Peripheral intravenous catheter is one of the most commonly used venous pathways in clinical treatment and care (Yeung et al., 2020). At present, 0.9% commercialized normal saline is the most common in the clinical lock solution for peripheral intravenous catheter, which can greatly reduce the workload of clinical nurses and reduce their working time, but the choice of lock solution of peripheral intravenous catheter has also been a controversial topic in clinical practice (Eghbali-Babadi et al., 2015; Roszell et al., 2018). In 2005, the systematic review (Shah et al., 2005) has shown that heparin cannot prolong the use of peripheral intravenous catheter compared with normal saline. In 2013, the systematic review (Kumar et al., 2013) has concluded that the use of peripheral intravenous catheter can statistically significantly prolong the use of heparin and reduce the

TABLE 1 The characteristics of included studies.

RCT	Sample size		Country	Setting	Population	Catheter size	Interventions	
	Normal saline group	Heparin group					Normal saline group	Heparin group
Arnts et al., 2011	46	42	India	NICU	Neonates	24G	Normal saline 0.7 mL, q8h	Heparin 10 U/mL, q8h
Dai et al., 2016	49	63	China	Respiratory department	1~12 years old children	24G	Normal saline 2 mL, q12h	Heparin 50 U/mL, q12h
Fu et al., 2016	120	120	China	Paediatric internal medicine department	3~48 months old children	24G	Normal saline 2 mL, before drug administration	Heparin 20 U/mL, before drug administration
Li et al., 2014	100	100	China	Paediatric department	1~5 years old children	24G	Normal saline 5 mL, before drug administration	Heparin 10 U/mL, before drug administration
Liang et al., 2019	36	53	China	Respiratory department	1~3 years old children	22G, 24G	Normal saline 2 mL, before drug administration	Heparin 10 U/mL, before drug administration
Xu, 2012	60	60	China	Respiratory department	2~12 months old children	24G	Normal saline 5 mL, before drug administration	Heparin 10 U/mL, before drug administration
Yang, 2013	29	29	China	Paediatric department	3~9 months old children	24G	Normal saline 5 mL, before drug administration	Heparin 20 U/mL, before drug administration
Zhou et al., 2016	64	64	China	NICU	Neonates	24G	Normal saline 5 mL, before drug administration	Heparin 10 U/mL, before drug administration
Zhou, 2016	50	50	China	Paediatric department	2.2±0.7	24G	Normal saline 5 mL, before drug administration	Heparin 50 U/mL, before drug administration

Abbreviation: NICU, neonatal intensive care unit.

FIGURE 2 Risk of bias graph.



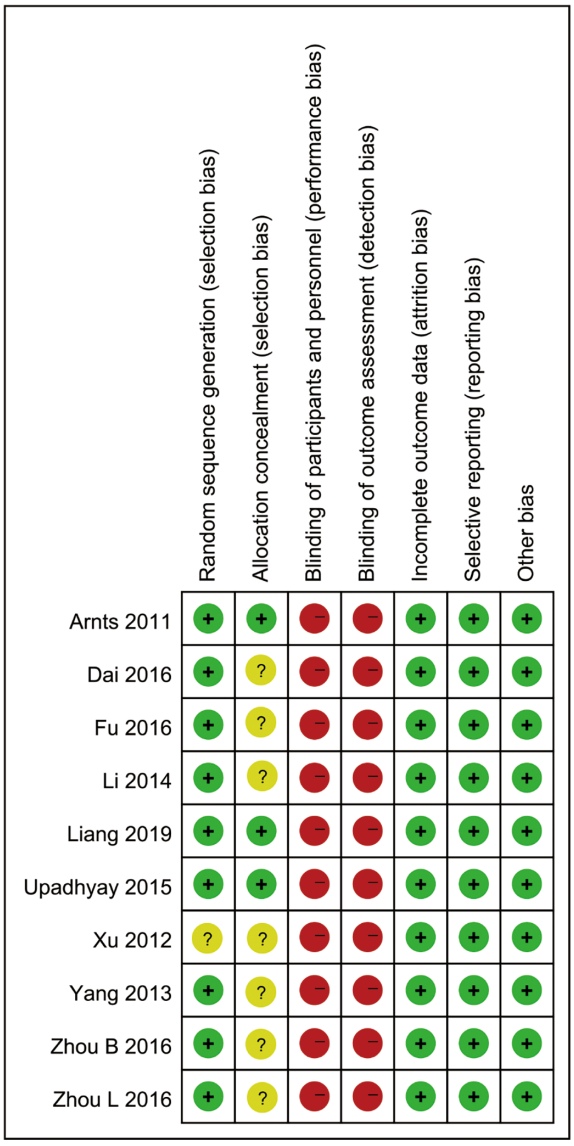
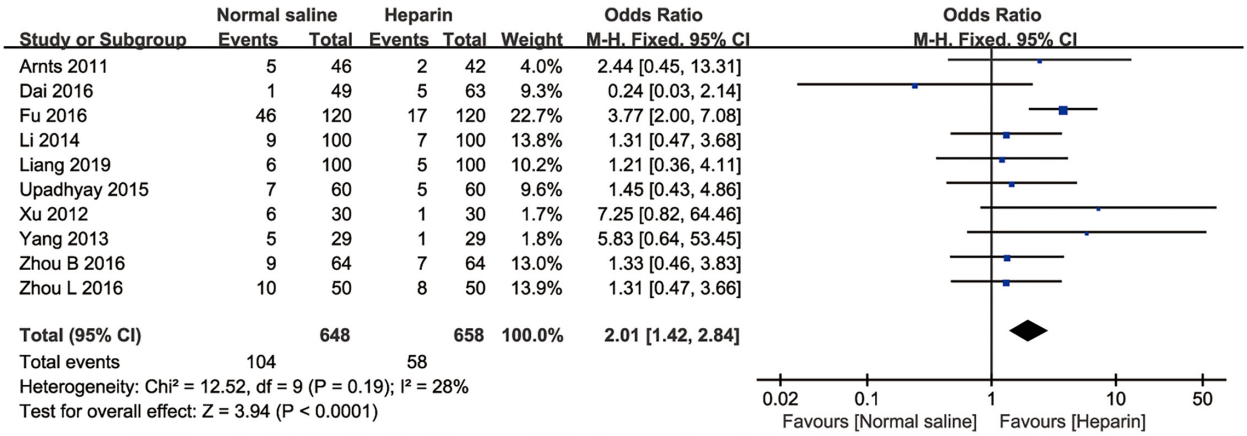


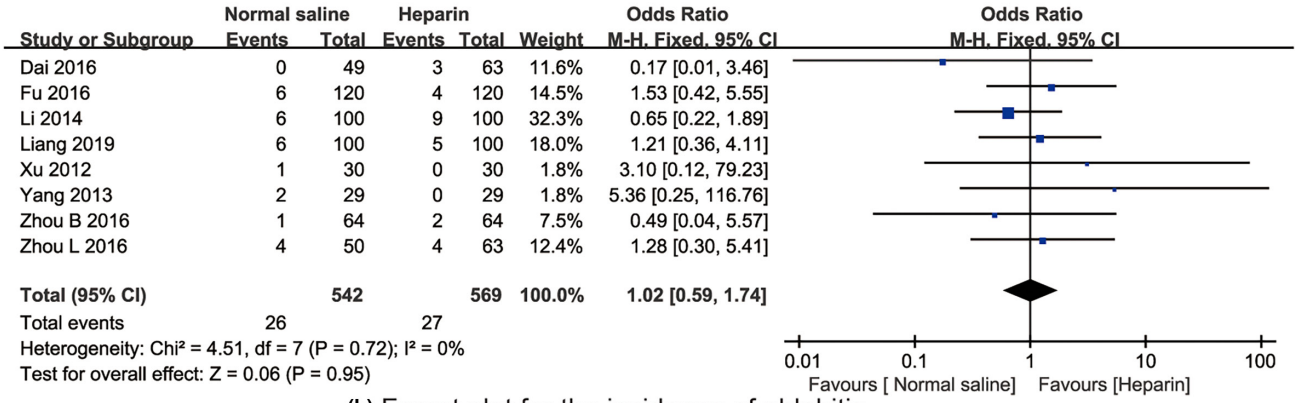
FIGURE 3 Risk of bias summary.

incidence of complications. The different conclusions above may be related to the number of included literatures and the age differences of the subjects, they have both included continuous infusion and intermittent flush studies, and the included children are mostly in 3–6 years old. In this study, three more recent RCTs are included, our results have shown that heparin reduces incidence of blockage of peripheral intravenous catheter and prolong the duration of peripheral intravenous catheter indwelling compared with saline lock for peripheral intravenous catheter, heparin may be more appropriate for the nursing care of peripheral intravenous catheter in children. However, there is no statistically significant difference in the incidence of phlebitis between heparin and normal saline. Heparin may be more beneficial and recommended for the nursing care of peripheral intravenous catheter.

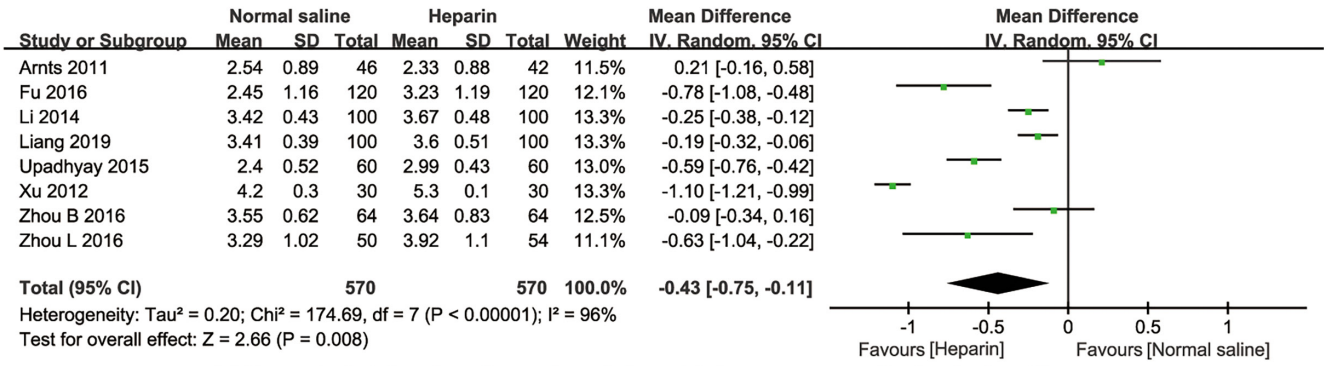
Peripheral intravenous catheter is a commonly used intravascular catheter, which is easy to operate and can be completed by nurses at the bedside. It is widely used in intravenous infusion treatment. According to statistics (Yan et al., 2019), the utilization rate of indwelling needle in China's tertiary hospitals is more than 99%. However, in clinical practice, it is very prone to catheter blockage, drug exudation, phlebitis and other complications. There are many reasons for these complications. This operation requires relatively high requirements for nurses, especially in paediatrics, because children cannot cooperate effectively, coupled with children's loose skin and fragile and sensitive veins, venipuncture is difficult, which must be paid great attention to (Garland et al., 2005; Uslu et al., 2010). It has been recommended that strengthen the professional training of nursing staff in the department, unify the standard, reduce the operation error, improve the success rate of puncture and reduce the incidence of local complications. The blockage of the catheter directly affects the indwelling time, and the selection of appropriate sealing solution is the key to reduce the incidence of blockage (Ullman et al., 2022). Some studies (Greene, 2021; Schroeder & Davis, 2020) suggest that the lock solution of peripheral indwelling needle in children should use normal saline because its osmotic pressure is equal to that of blood osmotic pressure. However, normal saline does not have anticoagulant effect in vivo, and mural thrombus may occur when using saline to seal the tube, especially in children with blood hypercoagulable state, there may be the risk of thromboembolism (Shah et al., 2002; Sotnikova et al., 2020). In recent years, there are many clinical studies on the use of different concentrations of heparin sodium saline to seal the catheter, and have confirmed its feasibility and safety. Heparin sodium has strong anticoagulant effect in vivo and in vitro, and intravenous use can reduce blood viscosity and prevent thrombosis (Ranch-Lundin et al., 2021).



(a) Forest plot for the incidence of blockage of peripheral intravenous catheter



(b) Forest plot for the incidence of phlebitis



(c) Forest plot for duration of peripheral intravenous catheter indwelling

FIGURE 4 The forest plots for synthesized outcomes.

Heparin sodium diluted with normal saline can be used as indwelling needle sealing solution, which can prevent blood coagulation caused by blood reflux.

The reason for the long retention time of the peripheral intravenous catheter with heparin lock may be that heparin sodium is a polysaccharide sulfuric acid vinegar anticoagulant, which is composed of D-glucosamine, L-iduronic acid and D-glucuronic acid. Sodium alginate diacetate has anticoagulant effect both in vivo and in vitro, prolongs clotting time, and can be used as venous indwelling needle sealing solution after dilution, which can prevent blood reflux from causing blood coagulation and prevent thrombosis after catheterization (Moss et al., 2021). It is worth noting that previous cases of heparin allergy have reported that if high concentration heparin sodium saline is widely used during tube closure, it may lead to bleeding or rare heparin-induced thrombocytopenia in children with coagulation dysfunction, which makes its clinical application questioned (Han et al., 2016). Many researchers are concerned about the complications such as coagulation system disorder caused by heparin sodium saline flushing. In fact, iatrogenic bleeding caused by heparin sealing is very rare, and the metabolic half-life of heparin is in 1 h–2 h (Niyyar & Lok, 2013). Some studies (Bovet et al., 2020; You et al., 2017) have found that heparin sodium salt solution as a sealing solution is safe and reliable, neither need to monitor blood coagulation function, nor cause damage to other functions of the human body. The occurrence of phlebitis is an important complication of peripheral

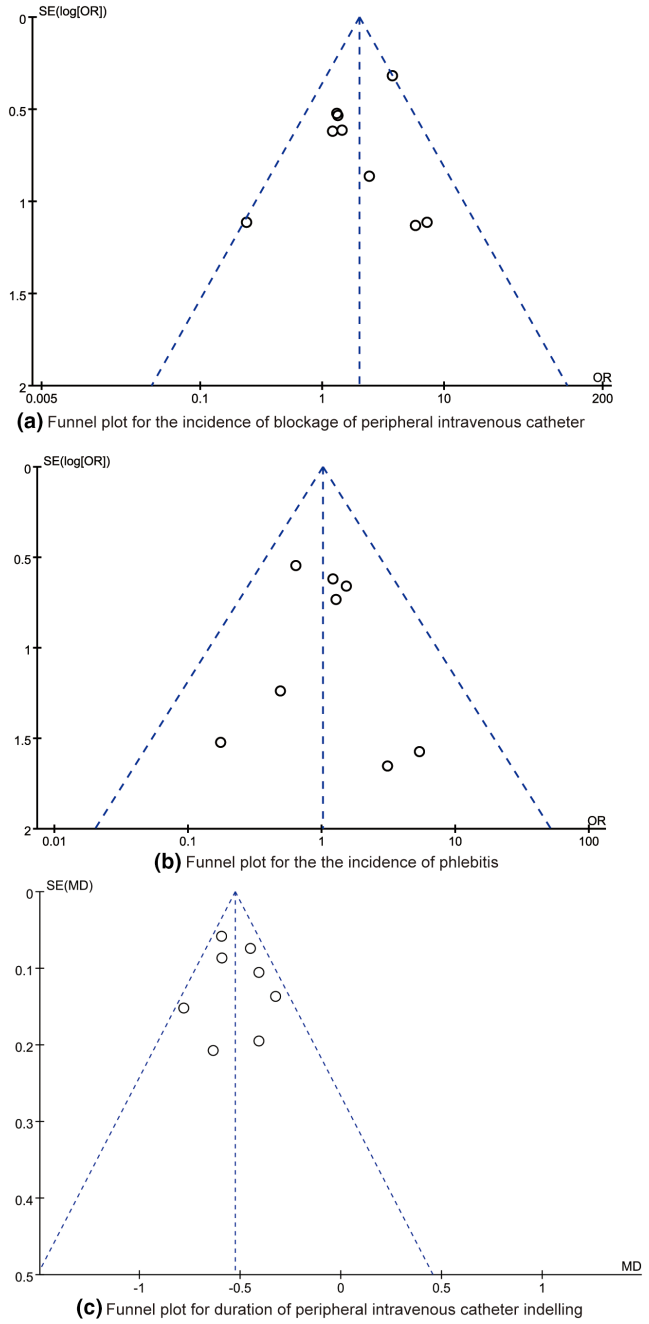


FIGURE 5 The funnel plots for synthesized outcomes.

intravenous catheter. The formation principle of phlebitis is that indwelling needle, as a foreign body, causes inflammation by mechanical stimulation and injury of vascular intima. Inflammation aggravates with the extension of indwelling time. (Zhong et al., 2017) At the same time, the occurrence of phlebitis is related to the configuration of sealing fluid, the compliance of aseptic principle in sealing operation, the personal hygiene of the children, and the condition of blood vessels (Rosenbluth et al., 2014).

There are some shortcomings and limitations in this meta-analysis. First of all, the sample size of the included RCTs is relatively small, and the statistical efficiency of the researches are limited. Secondly, the quality of the research included in RCTs is general, the design of blind research method is insufficient, and the outcome data may have some deviation. Thirdly, only Chinese and English literature reports are included in this meta-analysis, and there may be other grey literature or other language literature reports that are not included in the analysis. Besides, the majority of the included studies are conducted in China, which may affect the generalizability and applicability of the findings of this meta-analysis. Future studies with larger sample size and from different population and areas are warranted to analyse the role of saline and heparin on peripheral intravenous catheter.

5 | CONCLUSIONS

In conclusion, with 10 RCTs included, this meta-analysis has found that heparin lock is beneficial to reduce incidence of blockage of peripheral intravenous catheter and prolong the duration of peripheral intravenous catheter indwelling compared with saline lock, and there is no statistically significant difference in the incidence of phlebitis between heparin and normal saline lock. In clinical nursing, it is recommended to use heparin lock for peripheral intravenous catheter care when there is no coagulation dysfunction for children, which can effectively reduce the rate of blockage, prolong the duration of intravenous catheterization.

AUTHOR CONTRIBUTIONS

W Z, B W and D C designed research; W Z, B W, M C and D C conducted research; M C and D C analysed data; W Z, B W and M C wrote the first draft of manuscript; D C had primary responsibility for final content. All authors read and approved the final manuscript.

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FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this published article. The original data will be available from corresponding authors on reasonable request.

ETHICS STATEMENT

In this study, all methods were performed in accordance with the relevant guidelines and regulations. Research Ethics Committee approval and consent to participate are not necessary since our study was a meta-analysis.

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